OBSERVATIONS ON TREATMENT MECHANISMS IN PSORIASIS WITH SPECIAL REFERENCE TO TERRAMYCIN*

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The dramatic response (short of cure!) of two inveterate psoriatics to oral Terramycin† prompted a review of therapeutic experience with these two patients, covering respectively four and three and a half years. Both patients adhered to treatment and kept under observation with almost guinea-pig docility and faithfulness. Both showed repeated improvement under 1. low fat diet, pancreatin, thiamin and lecithin administration; 2. the intramuscular administration of whole boiled milk (grade B) as non-specific protein therapy; 3. Terramycin 1 to 2 grams daily.

Both patients illustrated the occurrence of the "virus-pyogen sequence" previously described by Stokes and Beerman (1) (including 2 other examples of its occurrence in psoriasis) as a mechanism of relapse. Both demonstrated the occurrence of light sensitivity (Stokes and Callaway (2)) to a particular spectrum, with Koebner phenomenon at the sites of light reaction, this notwithstanding the fact that in intervals between "virus" episodes, lamp and solar therapy seemed helpful. Both demonstrated the "wearing out" of even an initially very effective procedure, in prolonged use, and its renewed effectiveness on resumption after a prolonged rest period. Case 1 improved strikingly on undecylenic acid (Sevinon, Schering) and did so when it was used for additive effect after Aureomycin and Terramycin action had slowed down to a standstill. Case 2 obtained no benefit whatever from either Declid or Sevinon used alone and was unable to take Sevinon with Terramycin because of severe epigastric pain following each dose.

Case 1 demonstrated repeatedly the interrelationship of focal infection (throat and ear) to flares of psoriasis following operative intervention and spontaneously and post-"virus", probably streptococcal, focal exacerbation. Case 2 had a more typically "virus" type of trigger infection in his exacerbations.

Attention should be directed at this point, apropos the role of streptococcal infection in psoriasis, to the recent papers of R. Norrlund (3) and of H. W. Barber (4). Norrlund calls attention to psoriasis following hemolytic streptococcus infection, and Barber cites a number of instances of the acute onset of psoriasis or psoriatic crises following streptococcal infection of the throat and scarlet fever. He notes that the lag or latent sensitization period before the psoriasis appears is similar to that in rheumatic fever between throat and joint involvement (10 to 21 days).

As we hypothesize the sequences in these 2 cases, the streptococcal infection instruments the psoriatic flare reaction, while in some, but not by any means

* From the Graduate School of Medicine of the University of Pennsylvania.

† Kindly supplied by Charles Pfizer and Company, Incorporated, for investigative purposes.

Received for publication May 29, 1951.

all instances, the assumed virus infection instruments the streptococcal complication or sequela (virus-pyogen sequence, see Stokes and Callaway (2) and Stokes and Beerman (1)). The role of the antibiotic would more probably be in the control of the streptococcal (or other bacterial infection?) than in any action on the virus, if present.

Both of our patients were pulled out of what threatened to be complete exacerbative generalization following severe symptoms of the type commonly spoken of as "Virus X" (Coxsackie viruses or A_1 influenza?) by Terramycin, with arthritoid accompaniment in Case 2, the joint symptoms responding with the skin.

Improvement in Case 2 which had come to a standstill on 4 × 250 mgm. Terramycin daily, was apparently resumed when the dose was increased to 12 × 250 mgm. Terramycin daily.

Both patients had pathologic stool flora‡, including hemolytic B. coli, and Strep. viridans, and of paracolon bacillus in Case 1 and Shigella type organisms in Case 2. There was no change in the stool flora of Case 1 following improvement of psoriasis under the dosage of Terramycin used. Two yeast colonies in the cultures were thought to be of doubtful significance.

The highest estimated grade of improvement obtained was 80 per cent by the various methods used. This was reached in Case 1 with Sevinon. Improvement estimated at 65 per cent from a very bad exacerbative start (threatened generalization) was obtained in Cases 1 and 2 by Terramycin.

There was reason to suspect that Pyribenzamine given to relieve itching and flushing, contributed to improvement. Case 1 was given a trial of oral gentian violet and iodide without benefit. Combiotic and Sulfathalidine were tried with slight benefit. A startling general acceleration of improvement within a week while Case 2 was on Terramycin followed 35r unfiltered X-ray, to the top, back and each side of the head. Whether or not this had any influence on a focus of infection in the sinuses, which one of us (JHS) has suspected in several instances, remains hypothetical.

The marked though temporary good effects of foreign protein, undecylenic acid, and the broad spectrum antibiotics observed in these two psoriatic patients, and the correlation of exacerbations of the psoriasis with focal infective (streptococcal) and "virus"-like infective episodes, suggest to us the importance of infection or infection-allergy in psoriasis. Barber has suggested that psoriasis is a Selye type of reaction to stress of an infection. We had at first posited an intestinal infection as the focal source of an infection allergy, but the correlation of the flares in Case 1 at times with his extensive ear and throat infection, and his improvement under Aureomycin and especially Terramycin without recognizable change in his intestinal flora, suggests that the intestinal tract is by no means the only sensitizing focus, if it is a focus at all. Again, the dosage of Terramycin may have been too low materially to affect the intestinal flora. This man improved on undecylenic acid; his partner also with a pathologic

‡ The bacteriologic studies were carried out by Miss Anna Nichols of the Department of Research Surgery, Hospital of the University of Pennsylvania.

stool flora, did not. Attention has been called to the possible bacteriostatic and "antiallergic" properties of another fatty acid, propionic acid, in ophthalmologic practice, by Theodore (5).

The broad spectrum antibiotics are known to have nutritional and vitamin (B_{12} like) effects which may have contributed to the improvement secured with Terramycin in both patients. The action seemed rather rapid, however, to make this a sole explanation.

Finally, place must be given, we believe, to the psychosomatic aspects of psoriasis in interpreting therapeutic results. As in the atopic or eczema-asthma-hay-fever complex, suggestion plays a part in therapy. Each new approach, each new and reassuring medical attendant has for the moment, the cards stacked in his favor. Then as his successive efforts and devices fail to produce the hoped for cure, the patient loses heart and ground, only to regain it at the hands of a new enthusiasm or a quack formula. Very possibly this impact of suggestion by a proponent or enthusiast helps to explain the inability of skeptical followers to duplicate the results of an enthusiastic initiator. Observation of the color play of lesions in psoriatics, and the quieting effect of reassurance on a livid and pruritic eruption seems to support this impression of the suggestive element in treatment response.

The tolerance of Terramycin, used for months in a psoriatic erythroderma (Case 9 in Stokes and Beerman's series) was excellent. Its chief value up to this point for us is not curative, but as an aid in controlling exacerbations, if the exacerbation appears to be secondary to a pyogenic infectious process (ear, sinus, gastrointestinal tract, gall bladder, etc.) independent of or associated with a possible "virus" episode. It seems unlikely, as we have said, that Terramycin acts upon the supposed virus sensitizer in the so-called "virus-pyogen flare".

The multiple nonspecific factors which affect the course of the psoriatic, increase the difficulties encountered in evaluating any type of treatment.

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CASE I

S. G., male, age 26

1943—Strep throat, acute, then chronic ear. Still drains.
July 17, 1946—Onset of psoriasis in scalp.
Oct. 1946—Sudden rapid extension to body. Loss of 40 pounds weight; much depressed.
Oct. 1946—Salves, ultraviolet light, estrogens, autohemotherapy, calcium injections; low fat diet. No effect.

Jan.–May, 1947—Ultraviolet light, X-ray, intravenous and intramuscular injections, vitamins. Worse.

July 25, 1947 (JHS)—*Low fat diet, pancreatin*, lecithin. Emolients, starch baths, thiamin 30 mgm. t.i.d.

Sept. 8, 1947—Striking improvement, especially past 2 weeks. Morale improved.

Oct. 14, 1947—Stool bacteriology: B. coli, Clostridium, Strep. viridans, occasional Monilia, Candida type.

Dec. 8, 1947—Stationary. Put on *boiled milk injections*. Low protein diet, potassium iodide grains 10, t.i.d., Mazola.

Dec. 26, 1947—Little progress. Nitritoid reaction to milk controlled by atropin, divided dose, *Pyribenzamine*.

Feb. 7, 1948—Steady improvement under milk injections.

Mar. 4, 1948—Clearing rapidly on milk injections. Attack of urticaria. Milk continued.

Mar. 31, 1948—Coming to a standstill. Ultraviolet lamp, Desenex, anthralin added.

May 5, 1948—Astonishing improvement on lamp, Desenex, anthralin, milk.

June 22, 1948—Skin cultures: Strep. viridans, hemolytic Staph. albus. No Clostridium.

June 10, 1948—Steady improvement. *Dentist removed infected tooth.*

June 17, 1948—Flare of skin, accompanied by symptoms of "cold".

June 23, 1948—Demonstrable light sensitivity developed to spectrum of S-1 lamp. Koebner phenomenon, psoriatic lesion develops in situ on test.

June 30, 1948—Beginning to lose ground, previously effective treatment irritates. Chronic otitis lights up. Milk stopped. Niacin and B complex hypo begun.

July 18, 1949—Started on *gentian violet enseals, low fat, pancreatin, lecithin, potassium iodide.*

July 28, 1948—Beginning to flare again. All treatment suspended.

Sept. 22, 1948—Relapsed to original status or worse on starch baths, emolient and *pyribenzamine*.

Sept. 22, 1948—*Resumed milk injections, low fat diet* and *pancreatin, lecithin* and *thiamin*. Monilia never obtained from skin, only 2 colonies once in stool, possibility of moniliasis dropped.

Oct. 11, 1948—*Cold quartz lamp* resulted after negative skin test, plus anthralin.

Nov. 1, 1948—Fine progress, milk injections continued.

Nov. 22–Dec. 6, 1948—Astonishing gains. Mild nitritoids to milk, improves faster. *Pyribenzamine, autohemotherapy.*

Jan. 3, 1949—Another "cold". Flare of hands followed. Tonsillar residues, focal middle ear and sinuses implicated. Recovering from virus-pyogen flare. Boiled milk etc. continued.

Mar. 28, 1949—*Tonsil remnants and lymphoid foci removed.* Definite postoperative flare.

Apr. 4, 1949—Trunk begins to clear, hands still flaring.

Apr. 25, 1949—Hands still bad, sinus infection still active.

May 9–May 16, 1949—Light-sensitivity to hot quartz spectrum demonstrated. By May 16 a dermatitis had developed on the exposed surface; S-1 lamp test now negative.

June 1, 1949—Favorable progress resumed, *Niacin* added to milk injections, etc.

June 21, 1949—Back tolerates outdoor sunshine.

July 12, 1949—Miliaria from sun exposure. Psoriasis begins to spread again.

July 27, 1949—*Sevinon* (*undecylenic acid*) begun.

Aug. 10, 1949—Marked improvement, whole areas thinned and paled out, scale first increased then diminished. Sevinon continued at 8 capsules a day.

Sept. 21, 1949—Most remarkable improvement yet, reaching 65% in worst areas, on Sevinon.

Dec. 28, 1949—Improvement continues on 18 capsules daily, despite grippe in November with temporary flare.

Mar. 22, 1950—Still on 30 capsules Sevinon daily, condition stationary, occasional "cold" flares.

Apr. 5, 1950—*Sulfathalidine* added to Sevinon.

Apr. 19, 1950—Improvement resumed. Right ear draining. Sevinon stopped.
May 1, 1950—*Aureomycin* 2 x 250 mgm. 4 x daily, begun.
May 23, 1950—Improved further but not cleared by Aureomycin. Sevinon resumed.
June 1, 1950—Still on Aureomycin, and clearing.
Aug. 1, 1950—Flare following upper respiratory infection on last day of Aureomycin therapy.
Sept. 5, 1950—On "*Combiotic*" past 10 days. Psoriasis bad, only slight improvement.
Sept. 20, 1950—Stool, Strep. viridans, hemolytic Staph., 2 types paracolon group
Oct. 16, 1950—Sore throat, grippe, severe relapse of psoriasis. Annular lesions on face.
Oct. 16, 1950—*Terramycin* begun 500 mgm. 4 x daily.
Dec. 6, 1950—Remarkable clearing, exceeds 65% on 6 weeks of Terramycin. Trunk almost free.
Jan. 24, 1951—Improvement maintained but some flare followed re-appearance of ear discharge.
Feb. 14, 1951—Stationary or slightly regressing.
Mar. 6, 1951—Stool culture shows Strep. viridans and paracolon bacillus as in culture of Oct. 9, 1950, before Terramycin.
Mar. 12, 1951—"Flu" $2\frac{1}{2}$ weeks ago. Throat and ear symptoms. Definite exacerbation of psoriasis now in process. *Vitamin B-12 and folic acid* added to treatment.
Mar. 28, 1951—Without authority patient added Sevinon 15 capsules a day to the Terramycin and B-12. One week led to slight improvement.
Apr. 11, 1951—No change on dropping Sevinon. Resumed Terramycin, Sevinon and B-12—folic acid.
Apr. 27, 1951—Violent heartburn and "gagging" on attempting again to take Sevinon and Terramycin together. Stopped Terramycin.

CASE II

R. S., male, age 52. First seen November 1947. Psoriasis since 1920, syphilis 1939. Syphilis "cured" by As, Bi, "5-day drip". Blood and CSF negative.

1926—Psoriasis became generalized; widespread.
Oct. 1947—Fifty per cent improvement, due to Riasol or spontaneous.
Dec. 1, 1947—Anthralin and ammoniated mercury improves arms, hands.
Dec. 17, 1947—"Virus" flare with pustulation about mouth. "Cold" flares had been noted before.
Feb. 2, 1948—Tar and ultraviolet light (Goeckerman) failed.
Apr. 16, 1948—Worse and worse under starch baths and vaseline.
Apr. 19, 1948—*Boiled milk* intramuscularly begun.
Apr. 26, 1948—*Pyribenzamine* added for itching.
May 17, 1948—Much improved.
June 7, 1948—"Marvelous change for the better". Pyribenzamine stopped. No flare with gastrointestinal "virus" (?) infection.
June 28, 1948—Stationary. Tar and ultraviolet lamp resumed with further improvement. Boiled milk continued.
July 19, 1948—*Low fat diet, lecithin, Benadryl* at night.
Aug. 8, 1948—Eighty per cent cleared. Much sun exposure. Milk injections suspended.
Sept. 13, 1948—Only shins involved.
Oct. 18, 1948—Has a "cold", fall hay-fever also.
Nov. 22, 1948—Has held improvement but signs of pustular (virus-pyogen?) lesions.
Dec. 13, 1948—Definite recurrence, in process. Scalp involved.
Dec. 20, 1948—*Milk injections resumed.* Light sensitivity to cold quartz lamp demonstrated Koebner phenomenon.
Dec. 27, 1948—*Pancreatin-lecithin-thiamine-low-fat-diet* added.
Jan. 24, 1949—"The lesions are receding beautifully." Can tolerate R-S lamp.
Jan. 31, 1949—"Really remarkable."

Feb. 28, 1949—"Residue deserves trial of *undecylenic acid.*" Given Declid. All other treatment stopped.
Mar. 13, 1949—Somewhat of a flare. Taking 5 capsules Declid t.i.d.
Mar. 28, 1949—Definitely worse on undecylenic acid.
Apr. 4, 1949—Chronic respiratory infection; gastric upset from Declid.
Apr. 25, 1949—Eighth week Declid. Getting worse. On *boiled milk again.* R-S lamp resumed.
May 22, 1949—Improving. Reacts to boiled milk. Continuing Declid.
June 20, 1949—Condition so-so, 4 months on Declid. Boiled milk stopped.
July 18, 1949—Five months on Declid 5 capsules t.i.d. Psoriasis beginning to spread.
Aug. 1, 1949—Declid a failure. Stopped. Put on Sevinon.
Nov. 7, 1949—On 4 capsules q.i.d., improving.
Dec. 13, 1949—Sevinon produces no significant gains.
Dec. 17, 1949 to Nov. 6, 1950—Lapsed from observation, no treatment but cold cream, 11 months. Psoriasis stationary until 2 weeks ago when he had a severe "virus" infection.
Nov. 6, 1950—Psoriasis has flared, all old lesions recurred and extending, beginning arthropathy; scalp, face, neck, trunk and extremities heavily involved. Fever, neuromuscular pains, sinus infection etc. *Has had Aureomycin.*
Nov. 10, 1950—*Terramycin* begun 4 x 250 mgm. daily. Pyribenzamine 5 x 50 mgm. daily.
Nov. 14, 1950—Stool flora: hemolytic and non-hemolytic B. coli, aerobacter aerogenes, Strep. viridans, and an organism of the Shigella group. Two yeast colonies.
Nov. 17, 1950—Arthropathy less marked, toes and jaw. Eruption stops extending.
Dec. 1, 1950—Psoriasis begins to improve.
Dec. 15, 1950—Larger areas paling, new lesions scalp and face. *35r X-ray to front, back and sides of scalp,* forearms.
Dec. 22, 1950—"Amazing improvement all over body" within one week.
Dec. 29, 1950—Whole blood; third dose of X-ray to scalp.
Jan. 6, 1951—Original areas of involvement, including scalp and face, almost cleared. Previously free areas show small scattered new lesions.
Jan. 29, 1951—Same. Arthropathy much better.
Feb. 12, 1951—Stationary. Demineralization of foot bones shown by X-ray.
Mar. 5, 1951—Improvement maintained on 4 x 250 mgm. Terramycin daily.
Mar. 28, 1951—No further improvement. *Dose of Terramycin doubled* to 8 x 250 mgm.
Apr. 9, 1951—Further improvement, hands, shins, joints on 12 x 250 mgm. Terramycin.
Apr. 29, 1951—No further gain. The formerly normal areas are now involved as the old ones have cleared, but at that he's 60 per cent improved.
Apr. 29, 1951—Terramycin cut to 8 x 250 mgm. daily and Vitamin B-12 and folic acid (Rubrafoline) and Sevinon 2 capsules t.i.d. added.